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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,800	10/21/2003	Edmond J. LaVoie	735.038US2	5628

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EXAMINER	
MITCHELL, GREGORY W	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,800	LAVOIE ET AL.	
	Examiner	Art Unit	
	Gregory W. Mitchell	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the remarks and amendments filed December 01, 2004. Claims 10 and 24 have been amended. Claims 1-28 are pending and are examined herein.

Applicant's arguments regarding the 35 USC 112(1) rejection of all bis-benzimidazoles described is persuasive. Accordingly, the 35 USC 112(1) scope of enablement rejection of the Office Action dated June 30, 2004 is withdrawn in part. The 35 USC 112(1) rejection over the treatment of all cancers is maintained. The 35 USC 112(1) rejection as it pertains to the treatment of all cancers is provided below for Applicant's convenience.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of human T cell acute lymphoblastic leukemia, does not reasonably provide enablement for the treatment of all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all cancers are treatable by the bis-benzimidazoles described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention***:

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted bisimidazoles for the inhibition of cancer cells. The nature of the invention is complex in that it encompases the treatment of all types of cancers.

(2). ***Breadth of the Claims***:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of cancers by a bisimidazole.

(3). ***Guidance of the Specification***:

The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to inhibit any type of cancer cell is limited. All of the guidance provided by the specification is directed toward the treatment of specific cancers (RPMI, lymphoblastic leukemia, and CPT-K5, RPMI's camptothecin-resistent variant cell line) with one of four specific compounds.

(4). ***Working Examples***:

Applicant provides *in vitro* examples of the cytotoxicity of compounds 2 and 3 of Figure 1 versus RPMI, lymphoblastic leukemia, and its camptothecin-resistent variant cell line CPT-K5.

(5). ***State of the Art***:

While the state of the art is relatively high with regard to treating specific cancers, the state of the art with regard to treating cancer generally is underdeveloped. In particular, there is no known anticancer agent which is effective against all cancers. Carter, et al. (*Chemotherapy of Cancer*, 2nd ed., 1981) clearly teaches that for the forty known anticancer agents, none are effective against all cancers (pages 362-365). There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. This is true in part because cancers arise from a

wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Even those that affect a single organ are often not generally treatable. For example, the main types of lung cancer are small cell (oat cell), giant cell, clear cell, adenocarcinoma of the lung, squamous cell cancer of the lung, and mesothelioma. There is no such thing as a treatment of these generally because of their diversity. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

(6). ***Predictability of the Art***:

The invention is directed to inhibiting cancer cells in general. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). Cancers are especially unpredictable due to their complex nature. Please refer to the discussion of Carter, et al. and the state of the art in (5) that shows the different treatments of cancers. The treatment of one type of cancer could not be necessarily the same for the other type.

(7). ***The Quantity of Experimentation Necessary***.

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for inhibiting cancer cells. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of adminstration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. If again unsucessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any compound, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of cancer because, as described by Carter, et al., there is no known drug effective for inhibiting all types of cancer. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to inhibit cancer cells in a mammal by administration of one of the compounds within the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting cancer cells generally by administering the various bis-benzimidazole compounds of the claims is not considered to be enabled by the instant specification.

Response to Arguments

Applicant's arguments filed December 01, 2004 have been fully considered but they are not persuasive.

Applicant argues, "[i]t would be improper to maintain that undue experimentation is required for a skilled artisan to determine if a compound of the invention inhibits cancer cells because the specification actually provides the appropriate screen." This argument is persuasive as it pertains to the specific compounds of the invention, but is not persuasive as it pertains to the specific types of cancers of the invention. Applicant is claiming the inhibition of *all* cancers. A screening method does not enable one of ordinary skill in the art to inhibit all types of cancers, as instantly claimed, but merely provides an invitation to experiment.

Applicant argues, "Applicant's specification provides sufficient guidance to allow one of skill in the art to practice the claimed invention." This argument is persuasive as it pertains to the various compounds claimed because it is within the skill of the art to determine the efficacy of a given claimed but it is not persuasive as it pertains to all

cancers because the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the ***full scope*** of the claimed invention without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (emphasis added). Applicant has not provided sufficient guidance for one of ordinary skill in the art to be able to inhibit of *all types* of cancer cells.

Applicant argues, "[t]he instant specification ... contains working examples that clearly demonstrate that cancer cell growth can be inhibited using the claimed methods." This argument is not persuasive because what the working examples demonstrate is the inhibition of RPMI, lymphoblastic leukemia, and its camptothecin-resistent variant cell line CPT-K5, not cancer cells in general.

Applicant argues, "[c]ancer has been known for decades, has been well researched, and a variety of agents and methods are available to inhibit cancer cell growth." This argument is not persuasive because, as demonstrated by Carter et al., the inhibition of cancer cells *in general* is NOT known in the art.

Examiner stipulates that the skill in the art is high.

Applicant's arguments as they pertain to the predictability of the art is persuasive as it pertains to the enablement rejection of the various compounds. Applicant does not address, however, the predictability of the art of inhibiting cancer cells in general, however.

Applicant argues, "[t]he lack of a 'silver bullet' as stated in the last line of page 5 is irrelevant to the issue of enablement regarding the claimed invention." This argument

is not persuasive because Applicant's disclosure does not provide sufficient teachings to use the full scope of the invention. Carter et al. shows that while many compounds are known to inhibit some cancer cells, none are known to inhibit *all types* of cancer cells, as instantly claimed. Applicant's argument that Carter et al. is irrelevant because it provides "no chemical names or chemical structures for the numerous drug abbreviations and no data is provided to explain the nature of the heading 'Drug-Tumor Interaction'" is not persuasive because Carter et al. is used only to show that there are compounds that treat a range of cancers, but none that are effective against cancer generally or even a majority of cancers.

Double Patenting Rejection Maintained

Applicant's amendments have necessitated the withdrawal of the double patenting rejection of claim 10.

Claims 1-7, 12-21 and 26-28 remain rejected under the judicially created doctrine of obviousness-type double patenting over claim 1 of USPN 6221892 for the reasons set forth in the Office Action dated June 30, 2004.

Applicant's argument that one of ordinary skill in the art would understand the excluded –N(H)-C(H)=N- to include the exclusion of –N(H)-C(H)=N- substituted by oxo is not persuasive. Applicant has pointedly included that the carbons of R4 and R5 may, optionally, be substituted by oxo, but has not excluded –N(H)-C(H)=N- which has been substituted by oxo.

Applicant's suggested amendment to insert the phrase "optionally substituted by oxo" following the phrase "provided R4 and R5 taken together are not –N(H)-C(H)=N-" in claims 1 and 15 will overcome this rejection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm

SAEED PADMANABHAN
SUPERVISORY PATENT EXAMINER